Case Reports

Acute Hepatitis Associated With Colorado Tick Fever

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COLORADO TICK FEVER is an acute viral illness transmitted by bite of the wood tick *Dermacentor andersoni*. After an incubation period of from three to six days, chills, severe headaches, photophobia, myalgias, fever and leukopenia develop, lasting from five to eight days. Many patients experience a biphasic illness referred to as "saddle-back" fever. The initial symptoms may abate for one to two days, only to be followed by a recurrence of these symptoms for another two to four days before they subside. Although Colorado tick fever usually has a benign course and an excellent prognosis, in a few cases complications have been described, especially in children, of encephalitis, aseptic meningitis and hemorrhage.[1,2] Other associated syndromes have been pericarditis,[3] epididymo-orchitis, rheumatic fever syndrome and atypical pneumonitis.[4] In this case report the association of hepatitis with Colorado tick fever is described.

Report of a Case

A 67-year-old women presented in May 1983 with severe headaches, photophobia, myalgia, feverishness and chills for the past 24 hours. Three days before she had removed an attached wood tick. On examination she had conjunctival injection but no rash or fever. Her leukocyte count was 5,100 per μl with 75% segmented and 7% band forms. The presumptive diagnosis was Colorado tick fever, but because of the possibility of Rocky Mountain spotted fever, she received tetracycline, 500 mg, every six hours. Three days later she was admitted to hospital for supportive care because of increasingly severe symptoms and weakness. She said she had not taken aspirin, acetaminophen or medications other than tetracycline. She had had no exposure to blood products or persons with hepatitis. In the past she had had cholecystectomy.

Examination findings were unchanged from before, except for a temperature of 38.2°C (100.8°F). The following day her leukocyte count was 1,300 per μl with 38% segmented forms, 22% bands and 40% lymphocytes. Analysis of urine and chest x-ray film showed no abnormalities. Her serum aspartate aminotransferase level (glutamic oxaloacetic transaminase [SGOT]) was 204 units per liter (normal, 7 to 24); alkaline phosphatase, 87 units per liter (normal, 18 to 61); γ-glutamyl transferase (GGT), 234 units per liter (normal, 5 to 30), and bilirubin, 0.45 mg per dl (normal, 0.3 to 1.5). Blood cultures were negative for bacterial pathogens.

The tetracycline regimen was stopped. When her symptoms and fever resolved with supportive care over two days, she was discharged. Except for weakness, she felt well for five days, when right upper quadrant abdominal pain developed. When readmitted to hospital she was afebrile, but her liver edge was tender and palpable at the costochondral junction. There was no icterus. Laboratory values were as follows: hemoglobin, 15.0 grams per dl; leukocyte count, 7,100 per μl with 60% segmented forms, 2% bands and 38% lymphocytes; SGOT, 300 units per liter; serum alanine aminotransferase (glutamic pyruvic transaminase [SGPT]), 484 units per liter (normal, 4 to 25); GGT, 666 units per liter, and bilirubin, 0.9 mg per dl. The serum amylase level remained normal. A liver ultrasound study showed no biliary duct dilation. Tests for hepatitis B surface antigen, hepatitis B core antibody and hepatitis A virus antibody were negative. *Proteus* OX-19 agglutinins were negative and *Proteus* OX-K was 1:80. Serologic tests for brucellosis, leptospirosis, Q fever, Epstein-Barr virus and influenza A and B were negative. Cytomegalovirus titers and cultures were negative. Rocky Mountain spotted fever acute and convalescent titers were 64. Serologic test for acute Colorado tick fever by immunofluorescence antibody was less than 64, and convalescent titers were 2,048 or higher.

After two days her symptoms spontaneously resolved and SGOT, SGPT and GGT levels dropped to 78, 219 and 462 units per liter, respectively. Her recovery was uneventful, and all the enzyme values returned to normal within four weeks.

Discussion

This patient's clinical course was typical of Colorado tick fever except for the lack of "saddle-back" fever, which may be absent in as many as 52% to 58% of patients.[2,5] The diagnosis was confirmed by seroconversion of Colorado tick fever antibody. Other possible causes of hepatic inflammation were excluded. Although she received a short course of tetracycline by mouth, this drug is an uncommon cause of hepatic injury. When seen, tetracycline produces cholestatic features unlike the hepatocellular injury pattern seen in this patient.

In two extensive case reviews of the clinical and laboratory aspects of Colorado tick fever, hepatitis or abnormal liver function was not specifically sought.[2,4] In their review of 115 cases, Spruance and Bailey mentioned one child with Colorado tick fever-associated encephalitis and high-titer cold agglutinins who also had icterus and elevated SGOT levels.[2] Goodpasture and co-workers reported abdominal pain and vomiting occurring in about 20% of patients.[4] Hepatitis may have been present in some of these patients.

In the present case, hepatitis followed the initial acute phase of the illness. When Goodpasture and colleagues reported syndromes of epididymo-orchitis, rheumatic fever-like illness and atypical pneumonitis, they suggested that "circulating immune complexes may be the cause of the second phase of illness that many patients experience, as well as some of the unusual manifestations of the disease."[4] Per-

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haps the hepatitis in this patient may have been an immune complex manifestation.

There is little pathologic information about Colorado tick fever because human fatalities are rare. The virus is easily isolated from erythrocytes of most affected patients and from cerebrospinal fluid of those with central nervous system involvement. Viral replication occurs in bone marrow, lymph nodes, spleen, lungs, heart and liver of rhesus monkeys but without histologic abnormalities.[6] Identifying the virus in liver biopsy specimens or serum immune complex assays in future patients who have Colorado tick fever and evidence of hepatic dysfunction could determine if this association is primarily infectious or immunologic.

Colorado tick fever is a frequent disease in the mountainous western regions of the United States. More than 2,500 cases have been reported in the Rocky Mountain states in the past ten years, but the actual incidence is probably significantly higher (State Departments of Health of Montana, Idaho, Utah, Wyoming, Colorado and New Mexico, written communications, November 1983). With summer tourists returning home from endemic areas, this infectious disease can be seen nationwide.[4,7] Physicians should be alert to the possibility of hepatitis as an unusual manifestation of Colorado tick fever.

Addendum

Since submission of this manuscript, another patient was seen in whom serologically confirmed Colorado tick fever was complicated by thrombocytopenia (58,000 per μl), neutropenia (900 per μl) and elevated SGOT (42 units per liter) during the second phase of his biphasic illness. Analysis of serum immune complexes by Clq binding assay was normal (2 μg per ml). His recovery was uneventful.

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Cosyntropin Stimulation in Adrenal Vein Testing for Aldosteronoma

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ONCE A DIAGNOSIS of primary aldosteronism is established, it is necessary to distinguish between adenoma and hyperplasia. Aldosteronomas, comprising one half to two thirds of cases, are almost always unilateral. Surgical excision generally cures or improves the hypertension while preserving adrenal function. Hyperplasia is almost always bilateral. Even bilateral adrenalectomy usually fails to cure the associated hypertension, so that additional treatment is needed. Methods for identifying and localizing aldosteronomas include adrenal venography,[1-7] computed tomography,[1,8-12] adrenal isotopic scanning[1-3,13-17] and hormonal sampling via adrenal vein catheterization.[1-7,12,18] Adrenal venograms involve a risk of serious complications, including adrenal infarction and retroperitoneal hemorrhage. Computed tomographic (CT) scans and radioisotopic adrenal scanning fail to detect small aldosteronomas and occasionally produce false-positive results. The exact role of these two noninvasive tests remains to be defined. Adrenal venous sampling, with over 90% sensitivity,[1,12] sets the standard. Even this test, however, is subject to occasional error caused by episodic secretion of aldosterone.[18] To overcome this shortcoming, multiple sampling[18] and adrenocorticotropic hormone (ACTH)-stimulated sampling[1,3] have recently been advocated. The latter technique, the simpler and cheaper of the two, has not been directly compared with the standard technique of unstimulated adrenal vein sampling. The following case of primary aldosteronism, in which results of both the computerized tomographic scan and unstimulated adrenal vein sampling were inconclusive, documents the increased sensitivity of cosyntropin-stimulated adrenal vein sampling.

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Report of a Case

A 56-year-old man with chronic alcoholism was referred in February 1981 for evaluation of hypertension, hypokalemia and a 1-cm right adrenal mass seen on a CT scan. Mild hypertension was first noted in this patient in 1974 and diuretic therapy begun. Intermittent mild hypokalemia was attributed to his alcoholism and diuretic therapy. Cirrhosis of the liver was documented by liver biopsy three years before referral. The patient had been taking spironolactone (Aldactone)—150 mg a day—since one year before referral.

At admission, the patient's blood pressure was 135/90 mm of mercury with no orthostatic changes. Funduscopic examination showed arteriolar narrowing and mild arteriovenous nicking. The liver was slightly enlarged but not tender to the touch. No edema or ascites was present.

Results of routine laboratory studies showed normal values except for serum creatinine, 1.9 mg per dl (normal 0.7 to 1.4 mg per dl) and alkaline phosphatase, 141 units per liter (normal 35 to 115 U per liter). Serum potassium was 3.8 mEq per liter (normal 3.5 to 5.0 mEq per liter). Results of urinalysis were normal except for 1+ (10 mg per dl) protein. Administration of spironolactone was discontinued and a 200-mEq high-sodium diet begun. Primary hyperaldosteronism was diagnosed based on the following results obtained between days 12 and 14 of the high-sodium diet: (1) renal potassium wasting (60 to 66 mEq per 24 hours) despite the development of hypokalemia (2.7 to 3.1 mEq per liter); (2)